

Remarks

Applicants have canceled or withdrawn claims directed to the non-elected invention, without prejudice. Applicants hereby reserve the right to file one or more divisional applications to claim non-elected subject matter and subject matter set forth in canceled claims. Claims canceled to the extent that such claims relate to the elected invention have been canceled to expedite prosecution of the present case. Applicants have amended Claim 44 to incorporate the present elected genus. The amendment to the aliphatic linker is supported by the original application at page 35, at "aaa", as well as by the various branched examples, and original claims 31, 36, 37, and 41. The new claims are directed to Example 104 and Example 136 or salts thereof, as set forth in the originally filed application. Applicants maintain that none of the amendments introduce new matter and the amendments may properly be entered.

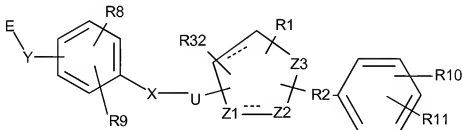
Applicants respectfully request entry of the amendments and reconsideration of the rejections in light of the following.

Response to Lack of Unity

Applicants gratefully acknowledge the telephone interview on July 30, 2007 with Examiner Chu regarding the election in accordance with the restriction requirement. Applicants agreed with the genus proposed by Examiner Chu as set forth in the present Office Action. Applicants understand that the remaining groups subject to restriction requirement are now final, and Applicants reserve the right to file one or more divisional applications to claim non-elected subject matter.

The elected and examined subject matter is as follows:

A compound, or a salt or solvate thereof of the Formula (I'')



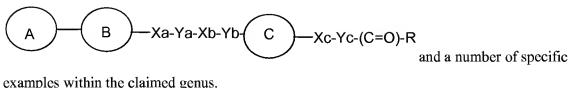
, wherein:

R2 is a single bond, and is bonded to Z3; X is a single bond; Y is a single bond; E is –CH₂COOH; R1 is H; R8 is H or alkyl; R9 is H or alkyl; R10 is CF₃; R11 is H; R32 is H, C1-C6alkyl, or C1-C6alkyloxy; U is an aliphatic linker replaced with an O; Z1 is C, Z2 is N, and Z3 is N; and the remaining substituents are as defined in original Claim 1. Applicants confirm election of the compounds of this genus.

35 USC 102

Claims 1-3, 16-20, 22, 25, 27-28, 32, 34-39, 41, 43-45, 47-49, and 52-54 stand rejected under 35 USC 102 (a) and (c) as allegedly being anticipated by Kimura et al. (WO 2003-JP6389 herein referred to as the '389, and in the corresponding family of Maekawana et. al. US 2006/0148858 A1, herein referred to as the '858 application).

The 858 application discloses a very broad generic formula (I):



Applicants have canceled most of the rejected claims without prejudice. Applicants respectfully submit that the remaining amended claims are novel wherein narrow and specific substituents are selected for the invention claimed herein. Further, none of the cited examples features the present substitution on the aliphatic linker.

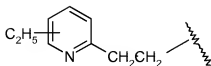
Applicants maintain that the amendments to the claims obviate the rejection under 35 USC 102. Applicants respectfully request reconsideration and withdrawal of the amendment under 35 USC 102.

35 USC 103

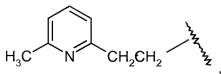
Claims 1-2, 16-20, 22, 25, 27-28, 32, 34-39, 41, 43-45, 47-49, and 52-54 are rejected under 35 USC 103 (a) as allegedly unpatentable over the '389 application.

Applicants respectfully disagree. Applicants note that the claims have been amended, and submit that the differences between the prior art and the claims of the instant case are non-obvious in light of the broad disclosure of the '389 application.

Examiner's attention is respectfully directed to a recent decision by the U.S. Court of Appeals for the Federal Circuit in Takade Chemical v. Alphapharm, 492 F.3d1350, 83 U.S.P.Q.2D 1169 (C.A.F.C. 2007). The issue before the court was whether a chemical moiety having a structural formula (i):



Should be considered obvious in view of prior disclosure of a chemical moiety having structural formula (2):



where both moieties were disclosed to have similar, albeit not identical, biological activities. The court affirmed the finding of non-obviousness by a district court.

The court began by noting that:

[i]n addition to structural similarity between the compounds, a prima facie case of obviousness also requires a showing of “adequate support in the prior art” for the change in structure. (492 F.3d 1350 at 1356, quoting *In re Grabiak*, 769 F.2d 729, 731-32 (*Fed. Cir.* 1985). Emphasis added.

The court noted that

[a] known compound may suggest its homolog, analog, or isomer because such compounds “often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties.” *Id.*

However, the court clarified that:

[...] in order to find a prima facie case of unpatentability in such instances, a showing that the “prior art would have suggested making the specific molecular modifications necessary to achieve the claimed invention” was also required. *Id.* (citing *In re Jones*, 958 F.2d 347 (*Fed. Cir.* 1992); *Dillon*, 919 F.2d 688; *Grabiak*, 769 F.2d 729; *In re Lahu*, 747 F.2d 703 (*Fed. Cir.* 1984). Emphasis added.)

Applicants further note that the C.A.F.C. opinion in Takada was issued after the decision by the Supreme Court in KSR International Co. v. Teleflex Inc., 127 S.Ct. 1727 (2007). The C.A.F.C. specifically noted:

[The] test for prima facie obviousness for chemical compounds is consistent with the legal principals enunciated in *KSR*. [...] Thus, in cases involving new chemical compounds, it remains necessary to identify some reason that would have led a chemist to modify a known compound in a particular manner to establish prima facie obviousness of a new claimed compound. (492 F.3d 1350 at 1356 and 1357.)

Turning to the compounds claimed by the present case. The disclosure of the ‘389 and ‘858 applications is exceedingly broad and in no way suggest that the presently claimed branching at the aliphatic linker would provide compounds having desired pharmacological activity. Compounds selected by the Examiner for comparison were specifically selected from among a

vast and divergent disclosure, through the use of hind sight reconstruction, and even this selection in no way suggest the branched linker claimed by the present application. Applicants maintain that the narrow genus of compounds claimed by this application is surprising and non-obvious as chemical compounds in an unpredictable field of art. Applicants respectfully submit that the '389 and '858 applications fail to satisfy the guidelines set forth in Takeda, and the present rejection may properly be withdrawn.

Finally, although the Examiner states that one must necessarily use hindsight in the obviousness analysis, Applicants submit that the obviousness analysis requires the Examiner to return to the time the invention was made, without the benefit disclosure of the presently claimed invention. The Examiner must view the prior art without reading the patent's teachings into the prior art. *Vandenberg v Dairy Equip. Co.*, 740 F.2d 1560, 224 USPQ195 (*Fed. Cir.* 1984). Applicants maintain that drawing knowledge of the present invention, when the prior art does not contain or suggest that knowledge, is to use the invention as a template for its own reconstruction, is an inappropriate process by which to determine patentability. The invention must be viewed not after the blueprint has been drawn by the inventor, but as it would have been perceived in the state of the art that existed at the time the invention was made. *Sensonic Inc. v. Aerosonic Corp.*, 81 F3d 1566, 38 USPQ2d 1551, 1554 (*Fed. Cir.* 1996). Further, as recently confirmed by Takeda: "it remains necessary to identify some reason that would have led a chemist to modify a known compound in a particular manner." (492 F.3d 1350 at 1356 and 1357). Applicants have not identified any teaching in the '389 or '858 applications to direct the skilled artisan chemist to prepare the compounds having branched aliphatic linker or the need to do so.

Applicants submit that the test for chemical obviousness delineated in Takeda has not been satisfied by the general disclosure of the '389 and '858 application. Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

35 USC 112

Applicants have canceled claims 52 and 53, obviating the rejection under 35 USC 112. Applicants courteously request reconsideration and withdrawal of the rejection under 35 USC 112.

Claim Objections

Applicants have amended the claims commensurate in scope with the elected genus. Applicants respectfully request rejoinder of the method of use claims, commensurate in scope with allowed compound claims. Applicants respectfully request reconsideration and withdrawal of the objections to the claims.

Conclusion

Applicants once again thank the Examiner for the telephone interview. Election of the invention of Group III is confirmed. Applicants reserve the right to file one or more divisional or continuation applications to claim non-elected or canceled subject matter.

Applicants have canceled or withdrawn the claims directed to the non-elected invention and certain claims directed to both the elected and non-elected invention for the purpose of furthering progress of prosecution. Applicants submit that no new matter is entered by the amendments to the claims and respectfully request entry of the amendments.

Applicants respectfully request favorable reconsideration in light of the above.

The Examiner is asked to contact the undersigned attorney for any matters relating to this application.

Respectfully submitted,

/MaCharri Vorndran-Jones/
MaCharri Vorndran-Jones
Attorney Agent for Applicants
Registration No. 36,711
Phone: 317-276-1665

Eli Lilly and Company
Patent Division
P.O. Box 6288
Indianapolis, Indiana 46206-6288

21 March 2008